Immature B-cell progenitors survive oncogenic stress and efficiently initiate Ph+ B-acute lymphoblastic leukemia.

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Public Summary:
Philadelphia chromosome-positive (Ph(+)) B-acute lymphoblastic leukemia (B-ALL) can initiate in committed B-cell progenitors. However, the stages of B-cell differentiation in which disease can initiate and the efficiency with which this occurs are unclear. We now demonstrate that B-cell progenitors, up to and including the pro-B cell, efficiently initiate Ph(+) B-ALL. However, cells at the pre-B-cell stage of development did not initiate disease. We show that this difference in leukemia initiating potential is due to the level at which the Arf tumor suppressor gene is induced in specific stages of B lymphopoiesis. Whereas immature B-cell progenitors survive the relatively low levels of Arf that are induced after oncogene expression, pre-B cells express the tumor suppressor gene at high levels and undergo massive apoptosis. These data demonstrate that the molecular events that control Ph(+) B-ALL initiation and tumor suppression in the B-cell lineage are developmentally regulated.

Scientific Abstract:
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